REMARKS

Claims 2-6, 8, 23-33, 37-40, 42, and 45-47 are pending in the application. Claims 23-33, 37-40, and 42 are withdrawn as being drawn to non-elected inventions. New claims 45 and 46 are added.

Claims 2 and 6 have been canceled and claims 3-5, 8 and 23 have been amended to recite the subject invention with greater particularity. Specifically, claims 3 and 4 have been amended to delete the term "derived" and now recite a composition. Additionally, claim 3 has been amended to depend from a non-canceled claim. Claims 5 and 8 have been rewritten in independent format and now recite that the fusion protein and composition, respectively, comprises HCV polypeptides and that the HCV polypeptides "consist" of an NS3, an NS4, an NS5a, an NS5b and a core polypeptide of HCV. Claims 5 and 8 have also been amended to clarify that the composition "activates HCV-specific T cells."

Withdrawn claim 23 has been amended to depend from claim 5, rather than canceled claim 2 in order to preserve Applicants' right to rejoinder.

Support for the foregoing amendments and new claims can be found in the original claims, as well as throughout the specification, for example, at page 2, lines 27-28, page 5, lines 17-18; page 15, lines 17-18; page 17, lines 18-20; page 18, lines 9-10; and page 30, lines 25-26.

The foregoing amendments are made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the canceled or unamended claims.

Nonstatutory Double Patenting

The Examiner maintained the provisional rejection of claim 2 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 41-44 of copending U.S. Patent Application Serial No. 10,612,884. The Examiner states: "Applicants admitted that the official terminal disclaimer will be filed..." Applicants wish to clarify that they never "admitted" that a terminal disclaimer would be filed. Rather, Applicants requested the rejection be held in abeyance until there was an indication of allowable subject matter.

Nevertheless, solely in an effort to advance prosecution, claim 2 has been canceled. Thus, this basis for rejection has been rendered moot.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 3-5 were objected to and rejected under 35 U.S.C. § 112, second paragraph, for depending on canceled claims. As explained above, claim 3 no longer depends from canceled claim 1 and claim 5 has been rewritten in independent format. Thus, this basis for rejection no longer applies.

Claims 3 and 4 were rejected based on the use of the term "derived." The Office argues: "Since the specification does not provide a standard for ascertaining the requisite degree of derivation and the term of 'derivation' has many interpretations, one of ordinary skill in the art would not be reasonably appraised of the scope of the invention." (Office Action, page 4.) Applicants note that the specification in fact describes HCV polypeptides "derived" from the HCV polyprotein, for example, at page 5. Nevertheless, in order to expedite prosecution, claims 3 and 4 have been amended to remove this term.

Claims 2 and 8 were rejected based on the use of the language "consisting essentially of" because "it is not clear if the claims are intended to exclude the presence of other polypeptides from the claimed fusion proteins." (Office Action, pages 4-5). Claim 2 has been canceled and claim 8 now recites that the composition comprises HCV polypeptides "wherein the HCV polypeptides "consist of" the recited components. MPEP §2111.03 explains that the claim language "consisting of" excludes any element, step or ingredient not specified in the claim. Moreover, when the phrase "consists of" appears in the clause of the body of the claim, rather than immediately following the preamble as here, it limits only the element set forth in that clause. The phrase does not exclude all other elements from the claim as a whole. See, e.g., *Mannesmann Demag Corp. v. Engineered Metal Products Col, Inc.*, 230 USPQ 45 (Fed. Cir. 1986). Thus, the compositions as claimed do not include HCV polypeptides from other regions but, as explained in the specification at pages 24-26, the compositions can include other non-HCV components in addition to the specified HCV polypeptides. Similarly, the fusion proteins present in the compositions of amended claim 5 do not include HCV polypeptides from other regions but, as explained at page 19, lines 15-18 of the specification, may contain other

sequences, such as sequences encoding amino acid linkers or signal sequences, as well as ligands useful in protein purification, such as glutathione-S-transferase and staphylococcal protein A.

Based on the foregoing, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

35 U.S.C. § 102

Claim 2 was rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Grakoui et al. (1996) *J. Virology* 67:1385-1395, Selby et al. (1993) *J. Gene. Virol.* 74:1103-1113 and Cheng et al. (1996) *Clinical and Diagnostic Virology* 6:137-145. Claim 2 has been canceled. Thus, these bases for rejection have been rendered moot.

Claims 2 and 8 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by PCT Publication No. WO 91/15771 to Houghton et al. ("Houghton-1") and U.S. Patent No. 5,683,864 to Houghton et al. ("Houghton-2"). Claim 2 has been canceled. Claim 8 recites a composition comprising HCV polypeptides, wherein the HCV polypeptides consist of isolated and purified HCV NS3, NS4, NS5a, NS5b and core polypeptides. The compositions of claim 8 further include a pharmaceutically acceptable excipient and an adjuvant.

With respect to both Houghton-1 and Houghton-2, the Office Action alleges:

> Houghton et al. teach that serological studies on HCV antigens that confirmed that no single HCV polypeptide is so identical that is immunological reactive with all sera. Therefore, the assay for detecting HCV should include 1st antigen from the C domain and at least additional HCV antigen domain selected from the group consisting of NS3, NS4, NS5. They further teaches that a NS5 antigenic peptide including NS5a and NS5b region.

(Office Action, pages 5 and 6.) Applicants respectfully traverse the rejections and the supporting remarks.

The law is clear that in order to anticipate a claim, a single source must contain all of the elements of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986). *Atlas Powder Co. v. E. I. du Pont De Nemours & Co.*, 224 USPQ 409, 411 (Fed. Cir. 1984). Moreover, the single source must disclose all of the claimed elements "arranged as in the claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989); *Connell v. Sears Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983). Finally, the law requires identity

between the claimed invention and the prior art disclosure. *Kalman v. Kimberly-Clar Corp.* 218 USPQ 2d 781, 789 (Fed. Cir. 1983, cert. denied, 465 U.S. 1026 (1984)). Applicants respectfully submit that the cited references do not teach or suggest all aspects of their invention, either explicitly or implicitly.

Neither of Houghton-1 or Houghton-2 describes the invention claimed in claim 8 or new claims 45 and 46 which depend thereon. In particular, Houghton-1 and Houghton-2 both fail to disclose compositions that activate HCV-specific T cells that include an adjuvant and HCV polypeptides that consist of NS3, NS4, NS5a, NS5b, and core, as claimed. Rather, Houghton-1 and Houghton-2 pertain to diagnostics **not** immunogenic compositions that activate T cells. Moreover, Houghton-1 does not disclose the particular species of fusion proteins used in the claimed compositions, namely fusion proteins with HCV polypeptides consisting of HCV NS3, NS4, NS5a, NS5b, and core. Houghton-1 lists fusions consisting of other combinations of antigens (see, *e.g.*, page 8, lines 21-26, page 29, page 35, lines 32-33 and page 37, lines 3-16).

Since Houghton-1 and Houghton-2 fail to teach each and every element of claim 8, these references do not anticipate claim 8 or claims 45 and 46 which depend from claim 8. For at least these reasons, withdrawal of the rejections under 35 U.S.C. § 102 is respectfully requested.

35 U.S.C. § 103

Claims 1-6 and 8 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Houghton-1 and PCT Publication WO 97/44469 to Valenzuela et al. (Applicants presume this is the intended reference). In particular, the Office Action alleges:

> [I]t would have been obvious to one of ordinary skill in the art at the time of the invention was filed to be motivated by the recited references and to combine the method taught by Houghton et al. and Valenzuela et al. in order to improve the selectivity and sensitivity of an antigen fusion peptide for detecting a biological sample that is possibly infected with any variable strain of HCV to make a fusion peptide antigen comprising different antigenic epitopes from different regions of HCV virus of an antigenic fusion peptide with different antigenic epitopes selected from different regions of different virus serotypes.

(Office Action, page 8). Applicants respectfully traverse the rejection under 35 U.S.C. § 103 and the supporting remarks on the following grounds.

To support an obviousness rejection under 35 U.S.C. § 103, "all the claim limitations must be taught or suggested by the prior art." MPEP § 2143.03. In addition, "the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure." MPEP § 706.02.

Initially, Applicants note claim 1 was previously canceled and claim 2 has been canceled herein. Applicants submit that the cited references do not disclose or suggest all the limitations of the remaining claims. Thus, a *prima facie* case of obviousness has not been presented by the Office.

As explained above, Houghton-1 relates to methods of diagnosis and reagents for use in these methods. Based on the Office's statements quoted above, the Examiner appears to recognize this is the case. The present claims, on the other hand, pertain to immunogenic compositions that activate T cells. There is absolutely no disclosure in Houghton-1 regarding such compositions. Not only does Houghton-1 fail to describe immunogenic compositions that activate T cells, the fusion proteins described are different than Applicants' proteins. See, e.g., page 8, lines 20-26 and page 37, lines 14-17 of Houghton-1. There is no disclosure or suggestion of a fusion protein consisting of NS3, NS4, NS5a, NS5b, and core HCV polypeptides. Finally, there is absolutely no reason to believe that a reagent useful as a diagnostic would also be useful for activating T cells.

The reference of Valenzuela fails to fill the gaps. As acknowledged by the Examiner, Valenzuela also relates to diagnostics and does not teach or suggest any fusion protein consisting of NS3, NS4, NS5a, NS5b, and core polypeptides (see Office Action, page 7). In particular, Valenzuela fails to disclose or suggest any fusion comprising NS5b or a composition that activates T cells. Like, Houghton-1, Valenzuela is simply not pertinent to immunogenic compositions that activate T cells. Rather, Valenzuela describes fusion proteins comprising multiple copies of equivalent epitopes for use in immunoassays.

Thus, the references when taken together do not disclose or suggest all the limitations of the present invention, and the Examiner has not met the burden of establishing a *prima facie* case of obviousness. In the absence of some teaching or suggestion in the cited references concerning immunogenic compositions that activate T cells and that include fusion proteins with HCV polypeptides consisting of NS3, NS4, NS5a, NS5b, and core polypeptides, as claimed in claims

3-5, or compositions that activate T cells with the specified HCV polypeptides as claimed in claims 8, 45 and 46, the Examiner has presented no more than an improper hindsight reconstruction of the present invention. As stated by the Court of Appeals for the Federal Circuit *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988): "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." Therefore, the Office has not met the requirements for a *prima facie* showing of obviousness under 35 U.S.C. § 103. For at least the above reasons, withdrawal of the rejections under 35 U.S.C. § 103(a) is respectfully requested.

CONCLUSION

In light of the above remarks, Applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

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